

PATENT COÖPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 23 JUN 2005

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/001750

International filing date (day/month/year)
19.02.2005

Priority date (day/month/year)
03.03.2004

International Patent Classification (IPC) or both national classification and IPC
C07D207/24

Applicant
DEGUSSA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/001750

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/001750

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-4
	No: Claims	
Inventive step (IS)	Yes: Claims	1-4
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-4
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V.

Relevant prior art is provided by

- (A) TETRAHEDRON 1997, 53(14), 5233-5254
- (B) TETRAHEDRON LETTERS 1992, 33(52), 8103-8104
- (C) JOURNAL OF ORGANIC CHEMISTRY 1981, 46, 3936-3938
- (D) US-A-6 103 910
- (E) JOURNAL OF ORGANIC CHEMISTRY 1983, 48, 1366-1368
- (F) TETRAHEDRON 1997, 53(2), 539-556
- (G) JOURNAL OF ORGANIC CHEMISTRY 2001, 66, 3593-3596

Novelty

The present claims appear to satisfy the requirements of Article 33(2) PCT vis-à-vis the cited prior art: The current process essentially differs from those of (A), (B), (F) and (G) on account of the aqueous one-phase system the oxidation is carried out in, and from (C)-(E) on account of the proline starting materials/products.

Inventive Step

The problem underlying the present application appears to be the provision of a further process for the oxidation of 4-hydroxyproline derivatives to the corresponding 4-ketoproline compounds.

(A) or (B) could be considered to represent the closest prior art. The current process essentially differs therefrom in that the ruthenium catalysis takes place in an aqueous one-phase system instead of in the two-phase systems disclosed in (A) ($\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ or $\text{CCl}_4/\text{CH}_3\text{CN}/\text{H}_2\text{O}$) or (B) ($\text{CCl}_4/\text{CHCl}_3/\text{H}_2\text{O}$). However, oxidation reactions with ruthenium catalysts in aqueous one-phase systems are already known as further standard possibilities, e.g. in acetone/ H_2O (see (C) or (D)) or in only H_2O , see (E). Consequently, when looking for further standard variations for the procedures of e.g. (A) or (B) the skilled person would automatically have taken the current process into account. An inventive step in the sense of Article 33(3) PCT could therefore only be acknowledged if the current process has an unexpected improved effect vis-à-vis the closest state of the art.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/001750